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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,602	03/15/2004	Nick Wan	5047 CON	1807

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GENZYME CORPORATION
LEGAL DEPARTMENT
15 PLEASANT ST CONNECTOR
FRAMINGHAM, MA 01701-9322

EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

10/800,602

Applicant(s)

WAN ET AL.

Examiner

Elizabeth Slobodyansky, PhD

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 1-5 and 12-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/27/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-17 are pending.

Election/Restrictions

Applicant's election with traverse of Group II, claims 6-11, in the reply filed on August 29, 2006 is acknowledged. The traversal is on the ground(s) that "Groups I, II and III do not represent distinct inventions. The claimed invention is directed to a method that utilizes a *Pichia pastoris* expression system to produce recombinant proteins with high-mannose carbohydrate structures. The inventions are interrelated and a search of the claims of Group II would necessarily include a search of the claims of Group I and III" (Remarks, page 4). This is not found persuasive because inventions I-III are patentably distinct because they are directed to materially different methods for the production of different products such as recombinant proteins, glucocerebrosidase and sphingomyelinase. Methods of inventions I-III use different products such as DNAs encoding structurally and functionally different proteins/enzymes and have different utility. Furthermore, the search of class 435, subclasses 195, 197, for example, while required for Groups I and III, is not required for Group II.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-5 AND 12-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups I and III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 29, 2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6-11 are directed to a method for the production of recombinant glucocerebrosidase or recombinant human glucocerebrosidase comprising culturing cells of *Pichia pastoris* which cells comprise a DNA molecule which encodes glucocerebrosidase (GCR). Therefore, the claims comprise the genus of DNAs encoding GCRs from any source and man made variants thereof as well as any allelic variant of human GCR.

As any chemical compound a DNA is described by its chemical structure. However, there is no description of the structure of any GCR or a DNA encoding thereof. Moreover, the specification fails to describe any other identifying characteristics or properties of DNAs encoding GCRs other than the functionality of encoding a GCR. Furthermore, it is known that humans have various allelic variants of GCR genes (e.g., Beutler et al., 1992, form PTO-1449 filed 1/27/05). Furthermore, there is no description of "high mannose carbohydrate structure" that is part of the requisite GCR

molecule such as the number of carbohydrate chains and their carbohydrate composition. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "high mannose structure". The specification does not define the number and composition of carbohydrate chains in said structure rendering the metes and bounds of the term unascertainable.

Claims 8 and 11 recite the limitation "wherein the cells are continuously cultured without the addition of molecular oxygen". This negative limitation defines the invention in terms of what it is not, rather than pointing out the invention rendering the metes and bounds of the claims unascertainable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman et al. in view of Invitrogen Catalog (1998).

Friedman et al. (US Patent 5,549,892, form PTO-1449 filed 1/27/05) teach that human GCR is needed for treatment of Gaucher's disease. They teach that it is an expensive form of therapy (column 1, lines 48-51). They teach the importance of GCR remodeling, i.e. its "high mannose structure" for the production of a pharmaceutically effective preparation. They teach the production of a remodeled recombinant human GCR in mammalian (CHO) cells.

Invitrogen Catalog (1998, form PTO-1449 filed 1/27/05) discloses the *Pichia pastoris* expression system and its "advantages over any other expression system" such as high expression levels, easy scale-up and inexpensive growth (page 19). It further discloses pGAPZ α vectors comprising a constitutive GAP promoter designed to express proteins constitutively in *P. pastoris* without the need for methanol. Invitrogen catalog teaches the advantages of said vectors (page 22). Apparently, these vectors are used in the instant invention (specification, page 25, line 8).

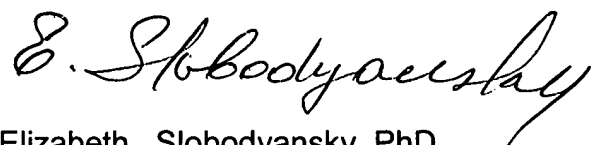
It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare recombinant human GCR with high mannose structure in *P. pastoris* cells using cells and vectors commercially available by Invitrogen. One of ordinary skill in the art at the time the invention was made would have been motivated to use *Pichia pastoris* expression system comprising pGAPZ α vectors for the

production of GCR in view of its therapeutic importance taught by Friedman et al. The advantages of *P. pastoris* system over expression in any other cells are taught by Invitrogen catalog. It would have been further obvious to use the continuous process in order to make the GCR production more effective and less expensive. pGAPZ α vectors allow for continuous production of the desired recombinant protein because no addition of methanol is required. Invitrogen catalog does not teach that the addition of molecular oxygen is needed for the protein expression in the *P. pastoris* system.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

September 27, 2006